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Award Number: W81XWH-07-1-0252

TITLE: Residential Segregation, Housing Status, and Prostate Cancer in African American and White Men

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REPORT DATE: April 2009

TYPE OF REPORT: Final

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for Public Release;
Distribution Unlimited

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REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. REPORT DATE *(DD-MM-YYYY)*	**2. REPORT TYPE**	**3. DATES COVERED** *(From - To)*
01-04-2009	Final	15 MAR 2007 - 14 MAR 2009

4. TITLE AND SUBTITLE

Residential Segregation, Housing Status, and Prostate Cancer in African American and White Men

5a. CONTRACT NUMBER

5b. GRANT NUMBER
W81XWH-07-1-0252

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)
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5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)

Henry Ford Health
Detroit, MI 48202

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)
U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

10. SPONSOR/MONITOR'S ACRONYM(S)

11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION / AVAILABILITY STATEMENT
Approved for Public Release; Distribution Unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT Racial-residential segregation which reduces the quality of housing has been proposed as a fundamental social cause of race disparities in health. This study, which included 378 African American and 496 white prostate cancer cases and controls, assessed housing status in relation to prostate cancer risk and aggressiveness and in relation to DNA damage in tumor and adjacent normal tissue. Housing built before 1950, a measure known to be associated with lead exposure in children, was the housing status measure most often associated with prostate cancer outcomes, in particular higher Gleason grade and stage of disease. When PAH adduct levels, a measure of DNA damage, was assessed, lower census tract home ownership was associated with lower PAH adduct levels in tumor adjacent normal tissue of African American men. Our findings suggest that housing may be a risk factor for prostate cancer aggressiveness and prostate cancer disparities and that lead exposure and PAH adducts may be two routes through which housing influences prostate cancer outcomes.

15. SUBJECT TERMS
Prostate cancer, African-American, housing, residential segregation

16. SECURITY CLASSIFICATION OF:			**17. LIMITATION OF ABSTRACT**	**18. NUMBER OF PAGES**	**19a. NAME OF RESPONSIBLE PERSON**
a. REPORT	**b. ABSTRACT**	**c. THIS PAGE**			USAMRMC
U	U	U	UU	43	**19b. TELEPHONE NUMBER** *(include area code)*

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I. Introduction

Race disparities in prostate cancer incidence and mortality are greater than for any other cancer in U.S. men and accounts for nearly 40% of all cancers diagnosed in black men (1;2). After much research, however, race, older age, family history of prostate cancer and residence in a western nation, remain the only consistently reported risk factors for the disease. This study examined race-based residential segregation as a potential cause (3) of racial disparities in prostate cancer occurrence and disease aggressiveness, using Fundamental Social Cause Theory (4). Fundamental social causes of disease are factors that influence access to resources that can be used to avoid disease or minimize the effects of disease once it occurs. Housing is one resource affected by residential segregation (3). In this study, the associations between individual homeownership and census tract housing (area ownership rates, percent of homes built before 1950, crowding, vacancy) and prostate cancer risk were assessed (Figure 1). In addition, among men with prostate cancer the association between housing characteristics and disease aggressiveness were evaluated. Aggressiveness was measured in three categories, prostate specific antigen (PSA >10) level at diagnosis, stage of disease (≥T2c) and histological grade of tumor (Gleason score ≥ 7). In addition, associations between housing characteristics and DNA damage as measured by polycyclic aromatic hydrocarbon (PAH) adducts were investigated.

Original Tasks included:

1. to determine whether selected *area housing and individual housing status (homeownership, housing density (crowding), and other housing factors such as age of structure and/or heating sources)* are associated with prostate cancer risk, age at diagnosis, and tumor aggressiveness and whether housing status is associated with observed racial differences in these prostate cancer outcomes.

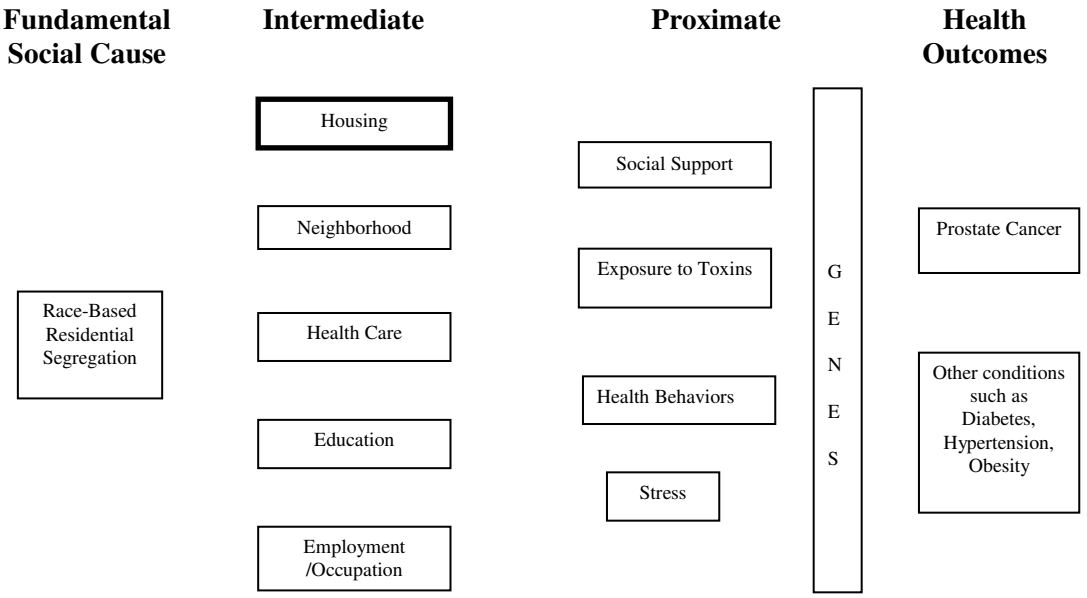
Final housing characteristics reported for this study include: individual homeownership, census tract (area) homeownership, census tract homes built before 1950 (proxy for lead exposure), census tract crowding (>1 person per room), and census tract home vacancy rates. Table 1 describes the hypothesized relationships between these housing measures and health.

2. to determine, through the use of factor analysis, whether *area housing and individual housing status*, is associated with prostate cancer risk, age at diagnosis, and tumor aggressiveness, through "latent factors" that include diet, physical activity, and genetic polymorphisms and whether those "latent factors" differ by race.

In year one it was determined that factor analysis was not the best approach as correlations between variables in some categories (example diet: calcium and vitamin D) were so high that it was difficult to identify "latent factors". Therefore a two-stage logistic regression approach was used which follows the model outlined in figure 1 and includes intermediate (neighborhood, education, employment/occupation) and proximal level co-variates (social support, exposure to toxins (occupational lead), and health behaviors). We also stratified by common comorbidities (hypertension(HTN), diabetes, obesity (BMI= body mass index), benign prostatic hyperplasia(BPH)) found in older men as these conditions have been associated with prostate cancer outcomes and all but benign prostatic hyperplasia were identified by Williams and Collins (2001a) as diseases that may also be the result of residential-segregation. This process and results are outlined under task 2.

3. to <u>begin</u> to test biological pathways through which *housing status* may impact prostate health outcomes; specifically, whether *housing status* is associated with markers of DNA damage (polycyclic aromatic hydrocarbons DNA-adducts (PAH)) and DNA stability (telomere content) in prostate tumor tissue and tumor-adjacent normal tissue of African-American and white cases.

Figure 1. Race-based residential segregation as a fundamental social cause of prostate cancer disparities



Housing Characteristic	route and/or health effects	Related references
Individual home ownership	non-homeowners have been documented to have more problems with heat, dampness, security. Inflammation and stress may be important	(5;6)
Area home ownership		
Housing built before 1950	lead based paint	(7), (8)
Crowding	infection, stress, and hormone levels	(9-13)
Vacant homes	lead and stress	(8;14;15)

Tables are presented at the end of each Task.

II. Body

Background and Patient Characteristics

Cases and controls used in this secondary analysis were originally enrolled in the *Gene-Environment Interaction in Prostate Cancer Study* (GECAP). The study population consists of African-American and white men who were patients in the Henry Ford Health System (HFHS), which provides medical care to between 20 and 30 percent of the metropolitan Detroit population. Eligible cases and controls used the HFHS as their primary source of health care, lived in the study area at time of recruitment, had no other serious medical problems that would preclude participation, and had no previous history of prostate cancer. Potential cases were identified after prostate biopsy or transurethral resection of the prostate (TURP) through the HFHS central pathology department and had a diagnosis of primary adenocarcinoma of the prostate. A stratified random sample of potential controls based on race (White or African-American) and five-year age group was drawn from the HFHS patient database such that the final enrolled sample was approximately 3 cases: 1 control. The over sampling of cases compared with controls was done because the primary objective of the original study was to evaluate gene-environment interaction using a case-only analytic approach (16). All study protocols were approved by the Henry Ford Hospital Institutional Review Board. Subjects were given a $50 stipend for participation in the original study. Between July 1, 2001 and December 31, 2004 the study attempted to enroll 863 men who had been diagnosed with prostate cancer within the last two years and 668 agreed to participate (77%). Of the 381 potential controls reached by telephone, 258 (68%) agreed to participate and 123 (32%) refused to participate. During the course of enrollment, eight cases and one control were found ineligible and 23 cases and 13 controls did not complete the study protocol, resulting in final study participation percentages of 75% (637/855) for cases and 64% (244/380) for controls.

Of 881 men in the parent study, 874 were self-identified as African-American or white and had a Michigan address for geocoding and mapping to census data for this study. Eleven residential addresses that did not initially match a census tract were resolved by correction of the address (i.e. avenue for street, apartment number in street address) or when determined to be correct but unmatched, were placed in a tract and block group by using web based mapping programs to identify street and cross streets. Because the addresses were used for mailings during the parent study and subjects confirmed current addresses during the study interview, it was assumed that addresses were real and no subjects were eliminated for having erroneous street addresses. One subject resided in a neighboring state and was removed because he did not live in the residentially segregated Metropolitan Detroit area. Figure 2 shows the distribution of study subjects in the Metropolitan Detroit area. African Americans (indicated by ★ in Figure 2) as expected are more likely to reside in Detroit than their white counterparts. As shown in table 1, cases and controls and black and white subjects did not differ by age. African-Americans were significantly more likely to be residents of Detroit and were less likely to own a home. African-Americans and whites differed significantly on all census tract housing factors which included percent of homes owned, percent of homes built before 1950, percent of homes with crowding (>1 person per room) and percent of homes vacant (Table 2). On average, African-American participants were more likely to live in census tracts with lower home ownership, higher percentages of older homes, and more crowded and vacant dwellings. Census housing measures were all modeled as continuous variables after being divided into quintiles. We found in initial descriptive analyses that distributions were skewed and that outliers tended to be of one race depending on the variable. For example, there were more African-Americans determined to be outliers on the variable census tract home vacancy. Since these outliers are real, census tracts with >50% vacancy, we did not want to exclude them from the analysis. In addition, transforming the independent variables would have proved to be difficult to interpret. Therefore, area housing measures were divided into quintiles and modeled as continuous variables.

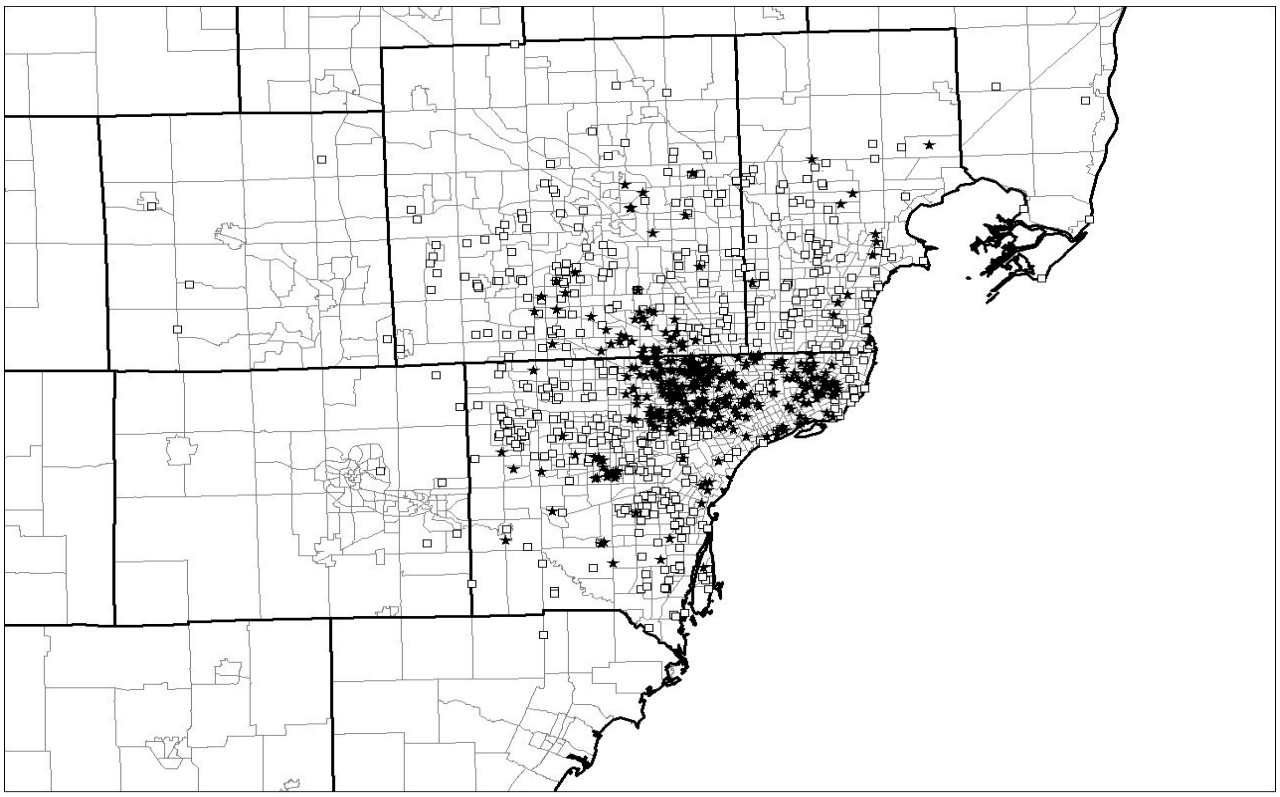


Figure 2. Geographic distribution of cases and controls

African-American cases and controls ★, White cases and controls □

Table 3 summarizes the intermediate level factors among cases and controls and by race. Although age (table 2) and insurance status did not differ across race, African American cases were more likely to be enrolled in Medicare or Medicaid that was not administered by an HMO (cases 27.6% vs. controls 15.1%, p=.036). Education at both the census tract and individual level (self-report) differed significantly by race. In addition, census tracts for African American subjects had higher unemployment than whites. However, black and white participants and cases and controls were equally likely to work in the manufacturing sector as their predominant employment and had a similar number of employers over their work history. With the exception of the percent of family headed households in a census tract, African American and white subjects different significantly on all other neighborhood factors, including median household income and male headed households. White cases had a significantly higher percentage of male headed households than controls but the relative difference (27.1% vs. 27.9%) was small. The percent black and percent white residents in tracts was not included in analysis as the majority of black participants lived in predominantly black neighborhoods (median 93.3% black and median 4.3% white) and the majority of white participants lived in census tracts with predominantly white residents (median 94.1% white and median 1.4% black).

Proximal level factors including health behaviors, lead exposure, marital status and genetic polymorphisms are reported for cases and controls in table 4. Cases had significantly more PSA tests and DREs in the one to four years prior to diagnosis or enrollment when compared to controls (PSA tests (mean ± sd):

cases 2.85 ±2.46 vs. controls 2.29 ±1.78, p=.001, DRE (mean ±sd): cases 2.68 ±2.31 vs. controls 2.21 ±2.09, p=.006). There were no racial differences in PSA and DRE testing in either cases or controls. In terms of reported dietary intake, fat intake (percent of total energy) was significantly higher in white controls when compared to white cases (36.4% vs. 34.7%, p=.035). African-Americans consumed less calcium and vegetables but significantly more selenium than whites. Vitamin D was marginally lower in African-Americans. Two-thirds of all men reported smoking regularly (66.2%) at some time in their life and after review by one of two industrial hygienists nearly the same proportion were determined to have had an occupational exposure to lead (66.6%). More African American controls reported ever smoking compared to race matched cases (76.4% vs. 65.8%, p= .046). There was no overall difference in rates of smoking by race, although African American controls were significantly more likely to report smoking when compared to white controls (76.4% vs. 59.6%, p=.006). Within men who were occupationally exposed to lead, 65.2% had respiratory lead exposure and 21.1% were determined to have cutaneous lead exposure while working. White cases had significantly higher mean years of lead exposure compared to race matched controls (7.9 ± 11.6 years vs. 5.4 ± 9.35 years, p=.027). On average African American cases had fewer years of occupation lead exposure than African American controls but this difference was not significant (5.90 ± 8.80 years vs. 6.61 ± 10.16 years, p=.50). There were no frequency differences between cases and controls on any of the genetic polymorphisms with exception of GSTM1 in African-Americans. There were significant frequency differences for all genetic polymorphism between races.

Prostate cancer is a disease of older men and comorbid conditions are prevalent in this age group. More than half (62.1%) of all study participants had a history of hypertension at the time of diagnosis (cases) or enrollment (controls) (Table 5). Diabetes was also prevalent with 18.7% of study subjects having medical record evidence of the disease. African Americans had significantly more hypertension and diabetes but did not differ from whites on BMI. A BMI ≥30 was most common among white controls. BPH was documented for nearly one third of all men and cases had significantly more BPH than controls. Cases were more likely to report a family history of prostate cancer in a brother or father than controls (21.2% vs. 13.2%, p=.006). However, it was determined that family history of disease would not be used in the analysis because data for African-Americans were more often unknown. Among African American men 20.2% did not know their biological fathers prostate cancer status compared to 11.1% of whites (p =.001). In addition, of 583 men who reported having at least one brother prostate cancer status was unknown for 9.1 % African-American reported brothers (62 of 684 brothers) compared to 5.0 % of white brothers (37 of 740 brothers). Family history of disease for African-Americans varied by as much as 20% across quintiles of median household income with lower rates of family history reported in the poorest quintiles.

In terms of aggressiveness of prostate cancer among cases, there were significantly more African-Americans with PSA greater than 10 ng/ml at diagnosis. Interestingly, older cases (>62 yrs) with high and low PSA at diagnosis did not differ in the number of PSA tests they underwent one to four years before diagnosis (PSA ≤10 ng/ml, 3.14 (sd ± 2.25) vs. PSA >10 ng/ml, 3.35 (sd ± 3.58)). However, younger cases and in particular younger African American cases with high PSA at diagnosis underwent fewer PSA tests than younger African American cases with low PSA at diagnosis (mean (± sd) PSA tests: 2.24 ±1.98 vs. 1.27 ±1.72, p=.03). Tables 2 through 5 summarize these findings.

Table 2. Prostate cancer case and control characteristics by race

	African American Control N=106	African American Case N=272	p-value		White Control N=136	White Case N=360	p-value		African American vs. White *p-value
Age (mean± sd)	61.6 ± 7.2	61.8 ± 7.4	.78		62.1±6.7	62.7 ± 6.6	.30		.08
Detroit Resident	77.4 %	70.6 %	.18		2.9 %	4.4 %	.45		<.001
Homeowner	76.4 %	72.1 %	.39		89.0 %	85.6 %	.32		<.001
Area Ownership	(%)	(%)			(%)	(%)			
Highest Q1	4.7	5.5	.36		31.6	31.9	.17		<.001
Q2	14.2	18.0			24.3	34.4			
Q3	22.6	14.3			18.4	13.9			
Q4	27.4	31.6			14.7	10.6			
Lowest Q5	31.1	30.5			11.0	9.2			
Built Before 1950	(%)	(%)			(%)	(%)			
Lowest Q1	7.5	9.9	.41		29.4	33.6	.22		<.001
Q2	9.4	6.2			28.7	23.6			
Q3	16.0	21.7			23.5	29.7			
Q4	31.1	33.1			11.0	6.4			
Highest Q5	35.8	29.0			7.4	6.7			
Crowding	(%)	(%)			(%)	(%)			
Lowest Q1	5.7	7.0	.74		30.9	35.6	.10		<.001
Q2	10.4	13.6			27.9	35.8			
Q3	16.0	13.2			22.8	15.6			
Q4	30.2	25.7			11.0	6.9			
Highest Q5	37.7	40.4			7.4	6.1			
Vacant	(%)	(%)			(%)	(%)			
Lowest Q1	7.5	12.5	.70		29.4	32.2	.92		<.001
Q2	14.2	12.9			25.0	21.4			
Q3	17.9	15.1			21.3	20.8			
Q4	24.5	25.0			16.9	17.2			
Highest Q5	35.8	34.6			7.4	8.3			

*p-value for difference between all African-Americans and all whites

Table 3. Intermediate level covariates for prostate cancer cases and controls

	African America Control N=106	African America Case N=272	p-value		White Control N=136	White Case N=360	p-value		*p-value race
Health Care									
HMO	67.9 %	56.6 %	.036		55.9 %	58.1 %	.15		.15
Commercial	17.0 %	15.8 %			26.5 %	19.2 %			
Medicare/Medicaid Without HMO	15.1 %	27.6 %			17.6 %	22.8 %			
Education									
% college in census tract (mean ± sd)	21.4±12.6	22.6±14.9	.45		35.0±18.4	37.8±19	.13		<.001
Self-Reported College Graduate	14.2%	23.9%	.009		38.2%	40.3%	.98		<.001
Employment/Occupation									
% Unemployed in census tract	11.0±5.1	11.2±5.9	.76		3.9±2.5	4.0±2.7	.71		<.001
Longest job held was in Manufacturing Sector	43.4 %	46.3 %	.61		37.5 %	42.8 %	.29		.22
Number of employers since age 18 (mean ± sd)	4.25 (1.98)	4.22 (1.90)	.86		4.68 (2.14)	4.36 (2.19)	.14		.12
Neighborhood (Average in Census Tract)									
Median Household Income	$38,015	$39,866	.37		$63,202	$65,306	.39		<.001
% Family Headed Household (mean ± sd)	84.8±9.1	85.4±9.2	.56		86.2±7.7	86.0±8.2	.86		.16
% Male Headed Household (mean ± sd)	18.6±5.5	18.5±5.5	.88		27.1±3.2	27.9±3.0	.014		<.001
% Below Poverty (mean ± sd)	18.5±10.5	18.6±11.5	.95		5.8±5.8	5.2±5.6	.34		<.001

*p-value for difference between all African-Americans and all whites

Table 4. Selected proximal level covariates in cases and controls

	African America Control N=106	African American Case N=272	p-value		White Control N=136	White Case N=360	p-value	*p-value
Health Behaviors								
PSA tests (mean, sd)	2.32 ±1.72	2.96 ±2.61	.019		2.26 ±1.84	2.77 ±2.33	.02	.34
DRE (mean, sd)	2.07 ±1.69	2.70 ±2.6	.011		2.33 ±2.35	2.63 ±2.12	.17	.96
Smoking - Ever	76.4%	65.8%	.046		59.6%	66.1%	.17	.17
Dietary Intake (mean, ± sd)								
Total Daily Calories	2411 ±1954	2428 ±1387	.92		2240 ±970	2333 ±987	.34	.18
Fat - % of Energy	35.5%	36.1%	.42		36.4%	34.7%	.035	.14
Vitamin C mg/day	139.6 ±165.7	128.8 ±105.6	.45		137.2 ±104.3	138.4 ±97.4	.90	.41
Vitamin D mg/day	5.87 ±5.36	6.17 ± 5.18	.63		6.57 ±3.87	6.77 ±4.72	.65	.06
Calcium mg/day	836 ±667	856 ±587	.78		1032 ±580	1044 ±613	.85	<.001
Selenium mg/day	149.9 ± 128.9	146.6 ± 88.4	.77		132.6 ±60.8	136.2 ±59.9	.56	.025
Zinc mg/day	15.03 ±13.3	14.9 ±9.1	.90		14.4 ±6.9	15.4 ±7.8	.20	.75
Alcohol	8.64 ±13.8	11.55 ±32.11	.37		9.37 ±15.1	13.66 ±24.7	.06	.31
Fruit servings / day	1.6 ±2.35	1.50 ±1.58	.63		1.42 ±1.37	1.57 ±1.32	.26	.99
Veg servings / day	1.50 ±1.13	1.64 ±1.21	.32		1.80 ±1.15	2.02 ±1.27	.08	<.001
Toxin- Lead (Pb) Exposure								
Occupational Pb	69.8%	69.5%	.95		61.0%	65.6%	.35	.10
Social Support								
Married	72.6%	71%	.74		75.0%	80.5%	.18	.01
Genetics								
AR_CAG								
<22	70.8%	72.1%	.80		50.7%	48.3%	.63	<.001
≥22	29.2%	27.9%			49.3%	51.7%		
AR_GGN								
<17	46.2%	46.3%	.25		11.0%	13.1%	.83	<.001
≥17	47.2%	50.7%			83.8%	81.9%		
Missing	6.6%	2.9%			5.1%	5.0%		
GSTP1								
II	28.3%	30.5%	.67		38.2%	43.1%	.33	<.001
IV/VV	71.7	69.5			61.7%	57.0%		
GSTM1								
present	62.3%	74.3%	.025		55.9%	47.2%	.08	<.001
absent	37.7%	24.6%			44.1%	52.8%		
Missing	0	1.1%			0	0		
Vit D_BSMI								
CC	56.6%	49.3%	.38		29.4%	35.8%	.18	<.001
CT/TT	43.4%	50.4%			58.1%	48.1%		
Missing	0	.4%			0	0		

*p-value for African American vs. White

Table 5. Clinical characteristics of cases and controls

	African American Controls N = 106	African American Cases N =272	p-value		White Controls N=136	White Cases N =360	p-value	*p-value
Hypertension	69.8 %	67.2 %	.62		53.7 %	59.2 %	.28	.002
Diabetes	20.8 %	26.6 %	.24		14.9 %	13.6 %	.71	<.001
BMI								
<25	15.1 %	21.7 %	.09		22.8 %	23.1 %	.01	.51
25-30	57.5 %	45.2 %			38.2 %	51.1 %		
>30	27.4 %	33.1 %			39.0 %	25.8 %		
BPH	16 %	31 %	.028		23.3 %	33.6 %	.003	.19
Gleason								
<7	--	42.3%			--	45.3 %		.65
≥7	--	57.0%			--	53.6 %		
Too small not able to score	--	0.7 %			--	1.1 %		
PSA at diagnosis								
≤10	--	79.4%			--	85.6%		.04
> 10	--	20.6%			--	14.4%		
Tumor Stage								
<T2c	--	72.1%			--	71.9%		.98
≥ T2c	--	27.9%			--	28.1%		

*p-value African American compared to white

Task 1

To determine whether selected *area housing and individual housing status (homeownership, housing density(crowding), and other housing factors such as age of structure and/or heating sources)* are associated with prostate cancer risk, age at diagnosis, and tumor aggressiveness and whether housing status is associated with observed racial differences in these prostate cancer outcomes.

As outlined for Task 1, associations between home ownership and census tract housing measures and prostate cancer risk and aggressiveness were assessed after adjusting for age and race (Tables 6a-d). Age at diagnosis was dropped as an outcome, when it was determined that a cohort would need to be established to complete this aim. This change was described in the Year 1 report. In place of age at diagnosis we added PSA level at diagnosis as an outcome. Originally, only stage and Gleason grade were listed as measures of aggressiveness.

Individual level home ownership (modeled for non-owner), census tract (area) home ownership (modeled highest to lowest quintile), percent of homes built before 1950 (modeled lowest to highest quintile), percent of homes with crowding (modeled lowest to highest quintile) and the percent of homes vacant (modeled lowest to highest quintile) were assessed in relation to each of the four prostate cancer outcomes. Logistic regression was used and because of multiple comparisons in both Task 1 and 2, we used the significance criteria suggested by O'Brien (17). Therefore, **a p-value ≤ .01 is considered significant and a p-value ≤ .05 is considered suggestive for significance**.

Tables 6a through 6d summarize the findings for Task 1 and for prostate cancer risk (6a) and disease aggressiveness (6b-d). Crowding was the only housing factor with probable association with risk of prostate cancer after adjustment for age and race (table 6a). Specifically in whites, increased crowding was associated with lower risk of disease (OR 0.84, CI .71-.99, p=.03). For the three prostate cancer aggressiveness outcomes, only housing built before 1950 was appeared to be associated with higher Gleason grade in whites (OR 1.20, CI 1.00-1.43, p=.047). Note the confidence interval includes 1.0, however.

Table 6a. Housing and risk of prostate cancer – Case-Control

	All N=874				AA N=378				White N=496		
	OR	CI	p-value		OR	CI	p-value		OR	CI	p-value
Home Ownership (No)	1.30	0.87-1.93	.20		1.26	0.75-2.13	.38		1.32	0.71-2.44	.38
Area Home Ownership ↓	0.93	0.82-1.04	.21		0.98	0.82-1.18	.85		0.89	0.77-1.04	.14
Built < 1950 ↑	0.92	0.82-1.04	.20		0.91	0.75-1.10	.34		0.94	0.79-1.10	.42
Crowding ↑	0.90	0.79-1.01	.08		0.97	0.82-1.15	.73		**0.84**	**0.71-.99**	**.033**
Vacant ↑	0.97	0.87-1.08	.61		0.94	0.80-1.11	.47		1.00	0.86-1.16	.99

* Adjusted for age and race, ↓= modeled as decreasing quintiles, ↑=modeled as increasing quintiles

Table 6b. Housing and risk of high Gleason score (<7 vs. ≥ 7) –Cases Only

	All N=626				AA N=270				White N=356		
	OR	CI	p-value		OR	CI	p-value		OR	CI	p-value
Home Ownership (No)	1.17	0.78-1.75	.44		1.14	0.66-1.97	.62		1.17	0.64-2.13	.62
Area Home Ownership (↓)	1.09	0.96-1.23	.20		1.07	0.88-1.30	.51		1.10	0.93-1.29	.27
Built < 1950 (↑)	1.11	0.97-1.26	.13		1.02	0.83-1.25	.88		**1.20**	**1.00-1.43**	**.047**
Crowding (↑)	1.10	0.97-1.25	.14		1.06	0.88-1.27	.57		1.14	0.95-1.37	.15
Vacant (↑)	1.06	0.95-1.20	.30		0.98	0.82-1.17	.83		1.14	0.97-1.34	.10

* Adjusted for age and race, ↓= modeled as decreasing quintiles, ↑=modeled as increasing quintiles

Table 6c. Housing and risk of high PSA at diagnosis (≤10ng/ml vs. >10ng/ml) –Cases Only

	All N=632				AA N=270				White N=362		
	OR	CI	p-value		OR	CI	p-value		OR	CI	p-value
Home Ownership (No)	1.36	0.84-2.21	.21		1.83	0.98-3.42	.06		0.79	0.33-1.86	.58
Area Home Ownership (↓)	0.96	0.81-1.15	.69		0.94	0.75-1.18	.58		0.99	0.77-1.27	.94
Built < 1950 (↑)	1.07	0.89-1.27	.48		1.06	0.83-1.34	.66		1.09	0.84-1.41	.50
Crowding (↑)	1.07	0.90-1.28	.44		1.10	0.87-1.40	.42		1.03	0.78-1.34	.85
Vacant (↑)	0.93	0.80-1.09	.36		0.90	0.73-1.11	.32		0.97	0.77-1.22	.80

* Adjusted for age and race, ↓= modeled as decreasing quintiles, ↑=modeled as increasing quintiles

Table 6d. Housing and risk of high tumor stage at diagnosis (<T2C vs. ≥T2C) –Cases-Only

	All N=632				AA N=272				White N=360		
	OR	CI	p-value		OR	CI	p-value		OR	CI	p-value
Home Ownership (No)	1.02	0.66-1.58	.93		1.10	0.60-1.99	.77		0.82	0.42-1.61	.56
Area Home Ownership (↓)	0.95	0.83-1.09	.48		.90	0.73-1.10	.30		0.98	0.82-1.18	.85
Built < 1950 (↑)	0.99	0.85-1.15	.89		1.06	0.84-1.33	.64		0.96	0.78-1.17	.68
Crowding (↑)	0.98	0.85-1.13	.76		0.88	0.72-1.07	.20		1.06	0.87-1.29	.59
Vacant (↑)	0.90	0.79-1.02	.09		0.93	0.77-1.13	.47		0.87	0.72-1.04	.12

* Adjusted for age and race, ↓= modeled as decreasing quintiles, ↑=modeled as increasing quintiles

Task 2

To determine, through the use of factor analysis, whether *area housing and individual housing status*, is associated with prostate cancer risk, age at diagnosis, and tumor aggressiveness, through "latent factors" that include diet, physical activity, and genetic polymorphisms and whether those "latent factors" differ by race.

Residential segregation in addition to affecting the quality of available housing also impacts health care access, quality of education, employment opportunities and neighborhoods. These intermediate level factors were adjusted for in Task 2 step 1. Backward logistic regression (Wald) was used to reduce the number of intermediate level variables. Separate models were run for all subjects and by race and for each outcome to ensure that variables important for both races and for risk and aggressiveness outcomes were included. In the second step of Task 2 proximal level variables were added and backward logistic regression was used again to reduce the number of variables included in final models. Table 7 includes the covariates included in final models for each outcome. In order to be included, variables had to remain in the final step of the backward regression model and be significant at $p \leq .05$. Additional variables were removed when correlations were higher than r^2=.80 (example: number of PSA and number of DREs were highly correlated). Comparing variables included in final models for each outcome, indicates that different intermediate and proximal level factors are important for each outcome. We also stratified by common comorbidities.

Table 8, at the end of this section, summarizes all findings for Task 2. "I" indicates an increased risk and significant at $p \leq .01$, "i" indicates increased risk at $p \leq .05$, "D" indicates decreased risk at $p \leq .01$ and "d" represents decreased risk at $p \leq .05$. Boxes have been shaded when sample sizes were too small to calculate associations.

Home Ownership (non-owner)

Not owning a home was associated with increased prostate cancer risk among all subjects with BPH (N=252, OR 12.23, CI 1.58-94.6, p=.016) and in African-Americans with BPH (N=100, OR 10.62, CI 1.03-109.5, p= .047) after adjusting for intermediate and proximal factors. White cases and controls had so few non-home owners with BPH that risk could not be evaluated for whites alone. The confidence intervals for all subjects and African-Americans were so wide that caution should be taken in drawing any conclusions from these findings. The only other significant findings for home ownership after adjusting for intermediate and proximal level factors occurred for the outcomes of PSA and stage at diagnosis. Among all cases without BPH, risk of high PSA was increased in non-home owners compared to homeowners (N= 424, OR: 2.02, CI: 1.08-3.77, p=.028). In all cases with lower BMI and lower BMI black cases, risk of late stage disease was increased (All N=134, OR: 5.41, CI: 1.80-16.29, p=.003 ; African American N=58, OR: 9.68, CI: 1.60-58.55, p=.01). Risk was also elevated in whites but was not significant (N=76, OR: 4.05, CI: 0.54-30.26, p=.17). Again sample sizes were small and results should be interpreted with caution. There were no important associations between home ownership and Gleason grade even after accounting for intermediate and proximal level covariates.

Area Home Ownership

Area home ownership was not associated with risk of prostate cancer, PSA at diagnosis or stage at diagnosis even after intermediate and proximal variables were included in models. Within all subjects with BPH

and African Americans with BPH, lower area home ownership was marginally associated with increased risk of high Gleason grade at diagnosis (All N=201, OR:1.29, CI 1.01-1.64, p=.04; African American N=82, OR 1.56, CI 1.02-2.39, p=.04; Whites N=119, OR 1.17, CI 0.86-1.61, p=.32).

Built before 1950

Older housing was not associated with prostate cancer risk among all subjects after adjustment for important intermediate and proximal factors. Within all diabetics , there was a 35% decrease in prostate cancer risk associated with each quintile increase in older housing (N=162, OR 0.65, CI 0.44-0.96, p=.031). Race specific findings were not significant but were also in the direction of reduced risk of cancer (African American N=93, OR 0.74, CI 0.42-1.31, p=.30 ; White N=69, OR 0.66, CI 0.36-1.19, p=.17). Increased older housing was also associated with higher Gleason grade at diagnosis among all non-hypertensive cases and white cases and approached significance in non-hypertensive African Americans (table 14). Among all cases risk increased with each successive quintile (Q) with the exception of quintile 4 and was significant for quintiles 3 and 5 compared to quintile 1 (Q2 OR 1.64, CI 0.67-4.01, p=.28, Q3 OR 2.97, CI 1.31-6.77, p=.009, Q4 OR 2.88, CI .90-9.17, p=.07, Q5 OR 11.12 CI 2.76-44.78, p=.001). In whites with high BMI or no BPH, risk of higher Gleason at diagnosis was increased with higher quintile of older housing. Housing built before 1950 was also associated with stage at diagnosis (table 15). In all cases and white cases with low BMI , having higher levels of older housing in a tract was significantly associated with reduced risk of late stage disease. African –American cases also showed reduced risk of late stage disease in those with low BMI but findings were not significant (OR 0.83, CI 0.40-1.76, p=.63). Interestingly for African Americans, when medium and high BMI categories were combined, the association between older housing and increased risk of late stage disease was nearly significant (African American medium and high BMI cases combined OR 1.44, CI 1.00-2.09, p=.053). Non-diabetic African American cases (OR 1.48, CI 1.04-2.11, p=.03) and those with no history of BPH (OR 1.54, CI 1.08-2.20, p=.018) were also at increased risk for late stage disease. There were no significant associations between housing built before 1950 and PSA at diagnosis once proximal factors were entered into models.

Crowding

The affect of crowding on prostate cancer outcomes was relegated to those with BPH in Aim 3. African-Americans with BPH living in more crowded housing were at increased risk for prostate cancer (N=100, OR 3.65, CI 1.15-11.59, p=.028). Risk was elevated for all subjects and whites as well but findings were not significant (All N=252, OR 1.28, CI 0.88-1.88, p=.20; whites N=152, OR 1.24, CI .77-2.01, p=.37). Higher quintile of crowding was also associated with higher Gleason score in all cases with BPH (OR 1.32, CI 1.02-1.70, p=.036), although race specific findings did not reach significance. Interestingly, in all cases with BPH crowding was associated with reduced risk of high PSA at diagnosis (N=204, OR 0.61, CI 0.38-0.98, p=.04). Crowding was not associated with stage at diagnosis.

Vacant Housing

As with crowding, associations with vacant housing and prostate cancer outcomes were significant only in those with BPH after adjustment for all important covariates. Among white subjects with BPH those living in neighborhoods with higher quintiles of vacant housing were at significantly increased risk of prostate cancer (N=152, OR 1.45, CI 1.01 -2.09, p=.045). Prostate cancer risk was also elevated but not significant in all BPH subjects and African-Americans with BPH living in census tracts with higher quintiles of vacant housing (ALL N=252, OR 1.30, CI .99-1.71, p=.06; African-American N=100, OR 1.57, CI .92-2.68, p=.10). Increased vacant

housing was also significantly associated with higher Gleason grade among all cases with BPH (N=201, OR 1.26, CI 1.01-1.58, p=.04). Vacant housing was not associated with PSA or stage at diagnosis.

Lead (Occupational) and Prostate Cancer Outcomes

Because housing built before 1950 was used as a proxy for neighborhood lead exposure and older housing was significantly associated with more prostate cancer outcomes than any other housing status measure, we examined the association between the covariate occupational lead exposure (any exposure, any respiratory exposure, and any cutaneous exposure) and prostate cancer outcomes. If occupational lead exposure was not associated with prostate cancer outcomes, then 1950 housing, a lower source of lead exposure in general, would likely not be the reason for associations between older housing and prostate outcomes. If occupational lead exposure is associated with prostate cancer outcomes, then older housing may be important to prostate cancer outcomes as an additional source of lead exposure. In Task 2 occupational lead exposure remained in final models for the outcomes of high PSA and high Gleason score. Tables 11a through 11d summarize occupational lead exposure and risk for each prostate cancer outcome taking into account the four genetic polymorphisms, androgen receptor GGN, glutathione-S-transferase pi (GSTP1) and mu (GSTM1), and Vitamin D receptor BSMI, that were identified as important covariates for prostate cancer outcomes in Task 2.

The androgen receptor is believed to play a role in prostate cancer development and progression. Two repetitive variants in the androgen receptor, CAG and GGN, have been studied in prostate cancer extensively, but with very mixed results (18-21). These repeat variants occur at different frequencies of length in blacks and whites. Most prostate research has focused on these variants ability to modify hormone levels, specifically androgen. Low levels of Vitamin D have also been associated with prostate cancer (22)and Kemp et al. (23) have reported that in urban children, higher levels of summer time Vitamin D, related to sunlight exposure, were associated with higher blood lead levels in young children. The Vitamin D BSMI polymorphism will be included in this study along with the CAG and GGN polymorphisms. Finally, polymorphisms of the glutathione-S-transferase (GST) family have been implicated in prostate cancer (24) . GST is a large family of phase II detoxification enzymes that are considered to be cancer markers because of their importance in the detoxification of substances with carcinogenic potential. Lead exposure has been shown to cause dramatic changes in expression of GSTs in rat kidney (25) and some GSTs detoxify polycyclic aromatic hydrocarbons (26), pollutants found commonly in urban environments. Two GST variants GSTP1 and GSTM1 will be included in analyses. The coding for these genetic variants is as follows: Androgen Receptor CAG (<22 repeats, ≥ 22 repeats) and GGN (<17 repeats, ≥ 17 repeats), Vitamin D BSMI (wild type/wild type vs. wild type/mutant vs. mutant/mutant), GSTP1 ile105val variant (wild type/wild type vs. wild type/mutant vs. mutant/mutant) and GSTM1 variant (present vs. absent). Only significant findings are reported.

For each prostate cancer outcome there was at least one genetic association that appeared to be affected by either the presence or absence of occupational lead exposure. In table 11a, African-American men who did not have a history of occupational lead exposure had increased risk of prostate cancer if they carried the long GGN repeat length (>22) polymorphism of the androgen receptor gene (OR 2.64, CI 1.02-6.79, p=.045). Among occupationally lead exposed African-American's, there was no difference in risk between subjects carrying the long GGN repeat and short repeat length (OR =80, CI .46-1.42, p=.45). In non-occupationally exposed men, the GSTM1 absent genotype was associated with lower risk of prostate cancer when compared to men carry the present allele. Again these associations were not found in men exposed to lead in occupational settings. Table 11b includes the significant associations identified for higher PSA at diagnosis. GSTM1 and GSTP1 polymorphisms show significant associations with PSA at diagnosis within unexposed men but not within lead exposed men. Table 11c includes the Vitamin D BSMI polymorphism and associations for high Gleason score at diagnosis. Lead exposed cases and lead exposed African-American cases carrying the CT or TT genotype had significantly higher risk of high Gleason score when compared to men carrying the CC genotype (All Cases OR

1.86, 1.22-2.84, p=.004, African American cases OR 2.98, CI 1.55-5.69, p=.001). Findings were not significant in those unexposed to lead, although risk was elevated. It should be noted that sample size was smaller in this unexposed group as well and may be a factor in these differences. Occupational lead exposure and stage at diagnosis findings are summarized in table 11d. The AR_GGN and GSTM1 polymorphisms were associated with later stage of disease. However for GGN the association with stage occurs in lead exposed men (All OR 2.15, CI 1.16-3.99, p=.015, African American OR 2.44, CI 1.14-5.26, p=.02) and for GSTM1 higher risk of late stage prostate cancer for men carrying the longer repeat polymorphism, occurred in men who were unexposed to lead. These results indicate that occupational lead status is an important modifier of several of the genes and polymorphisms commonly studied in prostate cancer, thereby, lending evidence to the hypothesis that older homes may also contribute to prostate cancer outcomes and disparities.

Lead (Occupational) and Common Comorbidities in Prostate Cancer Cases and Controls

Important findings from Task 2 occurred when results were stratified by comorbid conditions. Therefore, we assessed the association of lead with comorbidities in prostate cancer cases and controls (Table 12). Since the mid-1990s the association between lead and hypertension has been known (27) and data from the same study, the Normative Aging Study, also indicates that diabetes can modify the effects of lead (28). It is also known that lead can replace zinc in many biological proteins and a hallmark of BPH containing prostate tissue is high levels of zinc. In contrast, prostate tumor tissue is generally depleted of zinc. Therefore we examined whether there were associations between occupational lead and the common comorbidities in prostate cancer cases and controls. Table 12 shows that indeed within cases and controls occupational lead is associated with these comorbidities and interestingly these associations differ by prostate cancer status. This finding is consistent with the model of fundamental social causes of disease put forward by Link and Phelan (4) and modified by Williams and Collins (3;3) to include racial residential segregation. Although the African American and white men in this study did not differ significantly in their occupational exposure to lead, Table 2 shows that more than 60% of African Americans subjects lived in the two highest quintiles of older housing compared to approximately 8% of whites. Nationally, NHANES has shown that African American men have significantly higher blood lead levels than whites (29-31).

Summary Task 2

The case-only design of the parent study and the 3:1 case to control ratio may have reduced our ability to measure significant differences in risk of disease. We did identify associations between housing status and disease aggressiveness, however. Of the five housing status measures assessed, the percent of homes built before 1950 was the housing characteristic most often associated with prostate cancer outcomes, particularly the aggressiveness features of higher Gleason grade and higher stage at diagnosis. The other housing status measures were mainly associated with prostate cancer outcomes when BPH status was taken into account. Occupational lead was associated with polymorphisms commonly studied in prostate cancer and lead was associated with the common comorbidities in prostate cancer cases. These findings together indicate that older housing which has higher levels of lead may be associated with prostate cancer aggressiveness.

Table 7. Intermediate and proximal level covariates included in final regression models in Task 2

	Variable	Coding	Risk of Disease	Gleason ≥7	PSA >10ng/ml	Stage ≥T2C
Intermediate Level						
Health Care	Insurance status	Categorical (3)			X	
	Visits 1-4 years before diagnosis/enrollment	Sqrt transformation, continuous			(X)	(X)
Education	% less than high school	Sqrt transformation, continuous	X			X
	% college graduate	continuous	(X)			
	Self-reported education	Categorical (4)		X		X
Occupation/ Employment	% unemployed	Sqrt transformation, continuous				X
	Employment sector	Manufacturing vs. Non-Manufacturing				X
Neighborhood	% family households	quintiles used as continuous			X	
	% male headed households	quintiles used as continuous	X		X	
Proximal Level						
Health Behaviors						
PSA testing history	Count of PSA tests	continuous	X	X	X	X
DRE testing history	Count of DRE exams	continuous		(X)		(X)
Diet	Total Calories	tertiles	X			X
	Total fat % energy	continuous	X		X	
	Vitamin D-intake	tertiles		X	X	
	Calcium	tertiles				X
	Zinc-intake	tertiles		X	X	
	Alcohol	tertiles	X			
	Fruit5day	continuous			X	
Toxin exposures	Occupational Lead	No/Yes		X	X	
Genetic Variables	Androgen Receptor GGN repeat	<17 vs. ≥ 17				X
	GSTP1	II vs. IV/VV				X
	GSTM1	present vs. absent	X		X	
	Vitamin D BSM1	CC vs. CT/TT		X		

(X) Significant but excluded due to high correlation with another covariate

Table 8. Summary of findings for Task 2			CaP Risk			Gleason			PSA			Stage		
			All	AA	W	All	AA	W	All	AA	W	All	AA	W
Individual home ownership (Modeled as Non-Owner)	All													
	HTN	no												
		yes												
	DIAB	no												
		yes												
	BMI	low										I	I	
		medium												
		high												
	BPH	no							i					
		yes	i	i										
Area home ownership (Modeled as decreasing home ownership)	All													
	HTN	no												
		yes												
	DIAB	no												
		yes												
	BMI	low												
		medium												
		high												
	BPH	no												
		yes				i	i							
Housing built before 1950 (Modeled as increasing % of older homes)	All													
	HTN	no				I		I						
		yes												
	DIAB	no											i	
		yes	d											
	BMI	low										d		d
		medium												
		high						i						
	BPH	no						i					i	
		yes												
Crowding (Modeled as increasing)	All													
	HTN	no												
		yes												
	DIAB	no												
		yes												
	BMI	low												
		medium												
		high												
	BPH	no												
		yes		i		i			d					
Vacant (Modeled as increasing)	All													
	HTN	no												
		yes												
	DIAB	no												
		yes												
	BMI	low												
		medium												
		high												
	BPH	no												
		yes			i	i								

D =decreased risk of outcome and p≤ .01, d= decreased risk of outcome and p≤.05 , I =increased risk of outcome and p≤ .01, and i= increased risk of outcome and p≤ .05. Shaded boxes indicate associations that could not be evaluated because of small sample sizes.

Table 9. Housing built before 1950 (quintile increase) and risk of high Gleason grade (≥7) after adjustment for intermediate and proximal level variables

	All					African American					White			
Status	N	OR	CI	p-value		N	OR	CI	p-value		N	OR	CI	p-value
ALL	625	1.10	0.96-1.26	.19		269	0.99	0.80-1.24	.96		356	1.19	0.99-1.43	.07
HTN														
No	**234**	**1.46**	**1.17-1.82**	**.001**		89	1.40	0.95-2.08	.09		**145**	**1.58**	**1.16-2.14**	**.003**
Yes	390	0.92	0.76-1.11	.38		179	0.78	0.58-1.04	.09		211	1.02	0.79-1.32	.85
Diabetes														
No	505	1.11	0.96-1.29	.16		198	1.09	0.85-1.40	.49		307	1.15	0.94-1.39	.17
Yes	119	1.09	0.76-1.57	.65		70	0.86	0.50-1.46	.57		49	1.76	0.88-3.51	.11
BMI														
<25	141	0.94	0.70-1.26	.68		59	0.88	0.56-1.38	.57		82	1.16	0.75-1.77	.51
25-29	303	1.15	0.94-1.41	.17		121	1.11	0.78-1.58	.55		182	1.16	0.89-1.51	.26
≥ 30	181	1.20	0.91-1.59	.20		89	0.99	0.66-1.50	.97		**92**	**1.52**	**1.00-2.32**	**.049**
BPH														
No	423	1.13	0.96-1.34	.15		186	0.96	0.73-1.26	.75		**237**	**1.30**	**1.03-1.64**	**.027**
Yes	201	1.05	0.82-1.34	.68		82	0.92	0.61-1.39	.69		119	1.12	0.81-1.56	.50

Adjusted for age, (race), self-reported education, PSA tests 1-4 years before diagnosis, vitamin D intake, zinc intake, occupational lead exposure, Vit D_BSMI polymorphism genotype

Table 10. Housing built before 1950 (quintile increase) and risk of higher stage disease (≥T2C) after adjustment for intermediate and proximal variables

stage	All					African American					White			
Status	N	OR	CI	p-value		N	OR	CI	p-value		N	OR	CI	p-value
ALL	606	1.01	0.85-1.20	.90		264	1.32	0.97-1.79	.08		342	0.93	0.74-1.17	.53
HTN														
No	228	0.85	0.64-1.13	.26		88	1.37	0.75-2.53	.31		140	0.71	0.47-1.05	.09
Yes	377	1.18	0.94-1.48	.16		175	1.33	0.89-1.98	.16		202	1.20	0.88-1.64	.24
Diabetes														
No	490	1.01	0.84-1.21	.93		**194**	**1.48**	**1.04-2.11**	**.03**		296	0.91	0.71-1.16	.43
Yes	115	1.11	0.64-1.93	.71		69	0.63	0.19-2.07	.44		46	1.67	0.65-4.28	.29
BMI														
<25	**134**	**0.67**	**0.46-.98**	**.038**		58	0.83	0.40-1.76	.63		76	**0.53**	**0.29-.97**	**.039**
25-29	295	1.21	0.92-1.58	.17		118	1.75	0.96-3.18	.07		177	1.13	0.80-1.59	.48
≥ 30	177	1.08	0.76-1.53	.66		88	1.45	0.82-2.57	.20		89	0.90	0.53-1.51	.68
BPH														
No	413	1.13	0.93-1.38	.22		**182**	**1.54**	**1.08-2.20**	**.018**		231	1.04	0.80-1.35	.79
Yes	192	0.69	0.45-1.06	.09		81	0.36	0.11-1.19	.09		111	0.74	0.42-1.31	.30

Adjusted for age, (race), % less than high school in census tract, self-reported education, % unemployed in tract, employment sector (manufacturing vs. non-manufacturing), PSA tests, total calories, calcium, AR_GGN, and GSTP1

Table 11a. Occupational lead, genetic polymorphisms and risk of prostate cancer

	Risk	All						African-American						White				
Pb	Genotype	Control	Case	OR	CI	P		Control	Case	OR	CI	P		Control	Case	OR	CI	P
	AR_GGN																	
No	<22	28(34.1)	60(29.6)	1.52	0.82-2.80	.19		20(69.0)	41(50.6)	**2.64**	**1.02-6.79**	**.045**		8(15.1)	19(15.6)	1.00	.40-2.49	.99
	≥22	54(65.9)	143(70.4)					9 (31.0)	40(49.4)	.				45(84.9)	103(84.4)			
Yes	<22	36(24.7)	113(28.0)	.78	0.49-1.25	.30		29(41.4)	85(46.4)	.80	.46-1.42	.45		7(9.2)	28(12.7)	.68	.28-1.64	.39
	≥22	110(75.3)	290 (72.0)					41(58.6)	98(53.6)					69(90.8)	192(87.3)			
	GSTM1																	
No	present	48(56.5)	116(56.3)	1.04	0.61-1.78	.88		17(53.1)	67(81.7)	**0.26**	**.10-.65**	**.004**		31(58.5)	49(39.5)	**2.17**	**1.12-4.20**	**.02**
	absent	37 (43.5)	90(43.7)					15(46.9)	15(18.3)					22(41.5)	75(60.5)			
Yes	present	94(59.9)	256(60.5)	0.95	0.65-1.39	.78		49(66.2)	135(72.2)	0.74	.41-1.34	.32		45(54.2)	121(51.3)	1.16	.70-1.93	.56
	absent	63(40.1)	167(39.5)					25(33.8)	52(27.8)					38(45.8)	115(48.7)			

Adjusted for age, (race), smoking status, and alcohol consumption

Table 11 b. Occupational lead exposure, genetic polymorphisms and risk of high PSA (>10) at diagnosis

		All						African American						White				
Pb	Genotype	≤10	>10	OR	CI	P		≤10	>10	OR	CI	P		≤10	>10	OR	CI	P
	GSTM1																	
No	present	89(51.7)	26(78.8)	**0.17**	**0.06-0.49**	**.001**		53(79.1)	14(93.3)	0.26	0.03 - 2.28	.22		36(34.6)	12(66.7)	**0.07**	**0.01 - 0.39**	**.003**
	absent	82(48.0)	7(21.2)					14(20.9)	1(6.7)					68(65.4)	6(33.3)			
Yes	present	203(58.5)	49(68.1)	0.75	.42-1.33	.33		101(69.7)	32(80.0)	0.60	0.24 - 1.50	.27		102(50.5)	17(53.1)	0.90	0.42 - 1.94	.78
	absent	144(41.5)	23(31.9)					44(30.3)	8(20.0)					100(49.5)	15(46.9)			
	GSTP1																	
No	II	73(42.4)	5(15.2)	**3.41**	**1.20-9.66**	**.021**		22(32.4)	1(6.7)	8.83	0.99 - 78.9	.051		51(48.6)	4 (21.1)	2.10	0.54 - 8.21	.29
	IV/VV	99(57.6)	28(84.8)					46(67.6)	14(93.3)					53 (51.0)	14(77.8)			
Yes	II	134(38.5)	24(32.9)	1.24	.70-2.17	.46		45(30.8)	14(34.1)	0.80	0.37 - 1.76	.58		89(44.1)	10(31.3)	1.88	0.82 - 4.30	.13
	IV/VV	214(61.5)	49(67.1)					101(69.2)	27(65.9)					113(55.9)	22(68.8)			

Adjusted for age, (race), smoking, alcohol, Gleason grade and stage at diagnosis

Table 11c. Occupational lead exposure, genetic polymorphisms and risk of high Gleason score (≥7) at diagnosis

	Genotype	All						African American						White				
Pb	**VitD_BSMI**	<7	≥7	OR	CI	P		<7	≥7	OR	CI	P		<7	≥7	OR	CI	P
No	CC	37(40.2)	41(36.6)	1.33	0.77-2.32	.31		18(48.6)	16(35.6)	2.62	0.94-7.32	.065		19(34.5)	25(37.3)	.82	0.35-1.90	.65
	CT/TT	55(59.8)	71(63.4)					19(51.4)	29(64.4)					36(65.5)	42(62.7)			
Yes	CC	92(49.5)	91(38.7)	**1.86**	**1.22-2.84**	**.004**		51(65.4)	48(44.0)	**2.98**	**1.55-5.69**	**.001**		41(38.0)	43(34.1)	1.24	0.69-2.21	.47
	CT/TT	94(50.5)	144(61.3)					27(34.6)	61(56.0)					67(62.0)	83(65.9)			

Adjusted for age, (race), smoking alcohol, PSA and stage at diagnosis

Table 11d. Occupational lead exposure, genetic polymorphisms and risk of later stage disease (≥T2C) at diagnosis

	Stage	All						African-American						White				
Pb	Genotype	<T2C	≥T2C	OR	CI	P		<T2C	≥T2C	OR	CI	P		<T2C	≥T2C	OR	CI	P
	AR_GGN																	
No	<22	39(28.7)	20(30.8)	0.81	0.39-1.70	.58		28(51.9)	13(48.1)	0.83	0.30-2.30	.72		11(13.4)	7(18.4)	0.60	0.19-1.86	.38
	≥22	97(71.3)	45(69.2)					26(48.1)	14(51.9)					71(86.6)	31(81.6)			
Yes	<22	91(30.4)	19(19.0)	**2.15**	**1.16-3.99**	**.015**		69(51.1)	14(30.4)	**2.44**	**1.14-5.26**	**.02**		22(13.4)	5(9.3)	1.72	0.59-5.02	.32
	≥22	208(69.6)	81(81.0)					66(48.9)	32(69.6)					142(86.6)	49(90.7)			
	GSTM1																	
No	present	82(59.9)	33(49.3)	**2.39**	**1.13-5.04**	**.022**		47(88.7)	20(69.0)	**3.68**	**1.03-13.13**	**.044**		35(41.7)	13(34.2)	2.43	0.88-6.70	.09
	absent	55(40.1)	34(50.7)					6(11.3)	9(31.0)					49(58.3)	25(65.8)			
Yes	present	185(59.5)	67(62.0)	0.96	0.59-1.56	.85		97(69.8)	36(78.3)	0.73	0.31-1.72	.47		88(51.2)	31(50.0)	1.06	0.58-1.96	.84
	absent	126(40.5)	41(38.0)					42(30.2)	10(21.7)					84(48.8)	31(50.0)			

Adjusted for age, (race), smoking, alcohol, PSA and Gleason score

Table 12. Associations of occupational lead exposure and comorbid conditions in prostate cancer cases and controls

	Association with HTN			Association with Diabetes			Association with BMI			Association with BPH		
Occupational Lead Exposure	OR	CI	p-value	OR	CI	p-value	*OR_{LM} OR_{LH}	CI	p-value	OR	CI	p-value
Any (No lead vs. Any lead)												
prostate cancer cases	1.00	0.70-1.43	.99	**1.82**	**1.12-2.94**	**.016**	1.22	0.81-1.84	.34	1.26	0.87-1.84	.22
							1.42	0.88-2.27	.15			
prostate cancer controls	**1.81**	**1.03-3.19**	**.04**	0.73	0.36-1.48	.38	1.82	0.95-3.48	.07	0.64	0.33-1.25	.19
							2.77	**1.26-6.07**	**.011**			
Respiratory (No Resp lead vs. Any)												
prostate cancer cases	0.96	0.67-1.37	.82	**1.65**	**1.04-2.64**	**.04**	1.30	0.87-1.94	.20	1.25	0.86-1.80	.24
							1.46	0.92-2.33	.11			
prostate cancer controls	**1.88**	**1.07-3.30**	**.029**	0.76	0.38-1.56	.46	1.78	0.93-3.41	.08	0.68	0.34-1.32	.25
							2.90	**1.32-6.38**	**.008**			
Cutaneous (No cutaneous lead vs. Any)												
prostate cancer cases	1.07	0.71-1.63	.74	1.19	0.73-1.95	.49	1.25	0.79-1.96	.34	**1.90**	**1.27-2.86**	**.002**
							1.06	0.62-1.81	.82			
prostate cancer controls	0.98	0.50-1.89	.94	0.64	0.26-1.57	.34	1.13	0.55-2.35	.74	**0.30**	**0.11-0.81**	**.02**
							0.72	0.31-1.68	.45			

Adjusted for age and race. *OR_{LM} is for low (ref) vs. medium BMI and OR_{LH} is for low (ref) vs. high BMI N=632 for prostate cancer cases and 242 for prostate cancer controls.

Task 3

To <u>begin</u> to test biological pathways through which *housing status* may impact prostate health outcomes; specifically, whether *housing status* is associated with markers of DNA damage (polycyclic aromatic hydrocarbons DNA-adducts (PAH)) and DNA stability (telomere content) in prostate tumor tissue and tumor-adjacent normal tissue of African-American and white cases.

We used prostatectomy specimens, from 397 of the parent study prostate cancer cases who underwent surgery as their primary treatment, to determine if there were associations between housing status and DNA damage as measured by polycyclic aromatic hydrocarbon (PAH) adducts. DNA adducts are one of two pathway to DNA damage, the underlying cause of mutations that lead to cancer. The immunohistochemical methods for PAH adduct measurement with the BPDE (5D11) antibody have been previously described (32). We also measured telomere content as a marker of DNA damage in 27 prostate samples but the sample size was simply too small to adequately evaluate associations with housing status. For the housing status and PAH adduct analysis, we used backward stepwise (Wald) logistic regression as in Task 2 to reduce intermediate and proximal covariates. Further reduction of covariates was necessary based on the smaller sample size, therefore, we removed one of any two variables that had correlations higher than r^2=.65. As in Task 2 we considered findings with $p \leq .01$ to be significant and $p \leq .05$ to be a suggestive finding. Covariates that remained in final models are listed in Appendix 2. After adjusting for intermediate and proximal level covariates as well as age and race, we found that census tract (area) home ownership was the housing status measure that was most consistently associated with PAH adduct levels. In tumor-adjacent normal prostate tissue, lower area home ownership was associated with lower adduct levels in African- American men who did not have BPH (N= 123, OR 0.42, CI: 0.23-0.78, p=.006) and in men of normal BMI (BMI 25-29) (N=80, OR 0.23, CI 0.08-0.66, p=.006). Although not significant, we saw increased risk of high adduct levels in men with high BMI ($\geq$30) who lived in neighborhoods with higher quintiles of homes built before 1950 (All cases: N= 104, OR 1.76, CI 1.04-2.98, p=.033; African-American cases: N= 58, OR 2.24, CI 1.04-4.85, p=.04; White: N= 46, OR=2.22, CI 0.63-7.80, p=.22). There were no significant findings for adducts in tumor tissue.

At present our data set does not provide clues as to the reasons for associations observed between lower home ownership and lower adduct levels in normal tissue of African-American cases. Therefore, we plan to randomly select five low ownership census tracks and five high ownership census tracts of African-American cases and will qualitatively assess potential differences in PAH sources. The association for higher adducts in obese men living in older housing was a suggestive finding and may be of interest since lead and PAH are known to co-occur. For example combustion sources may produce PAH while at the same time dispersing lead. Before the 1980's this would have been the case for auto emissions.

In the process of conducting this multivariate analysis we also found two associations not previously reported. Among African-American cases, those in the highest tertile of zinc consumption were at increased risk for high PAH adduct levels in tumor-adjacent normal tissue when compared to the lowest tertile of zinc consumption (N= OR 1.66, CI 1.12-2.47, p=.011). Zinc has been shown to activate the production of 3-nitrobenezanthrone adducts in vitro (33). 3-nitrobenezanthrone is a nitro-PAH and potent mutagen found in diesel exhaust and ambient air particulate matter, especially in urban areas (34) . Zinc is capable of reducing the nitrogen component of nitro-PAHs thereby activating their carcinogenic potential (33). The PAH antibody used for this study is not expected to associate with nitro-PAHs although it is a non-specific antibody for BPDE adducts. Future studies of prostate cancer disparities should examine zinc and PAH- and nitro-PAH adducts.

In addition, in white prostatectomy cases, we found that the vitamin D receptor polymorphism BSM1 genotype CT/TT was associated with reduced risk of high PAH adduct levels in tumor tissue (N=223, OR 0.52 CI 0.30-.92, p=.025) but not matched normal adjacent tissue (N=223, OR 0.77,CI 0.44-1.35, p=.37) when compared to the CC genotype. After stratification by occupational lead exposure, this association remained significant only among white cases with no occupational history of lead exposure (No occupational lead exposure: N=78, OR 0.25, CI 0.09-0.72, p=.01, Occupational lead exposure: N=145, OR 0.78 CI 0.38-1.59, p=.49). This finding remained significant even after adjustment for occupational exposure to PAH, dietary intake of PAH, smoking, Gleason grade, and age. The BSMI polymorphism was not associated with adducts in African-American cases which is interesting since, we propose that African-Americans are likely exposed to higher levels of lead in their homes and neighborhoods and not just through occupational exposures. Perhaps the difference in findings by race is related to differences in lead exposure. Although occupational lead exposure alone was not associated with PAH adduct levels. Some studies have shown that the BSMI T allele is associated with higher bone and blood lead levels in lead exposed workers (35;36) and one study in HepG2 cells indicated that lead inhibits PAH induction by inhibiting genes that metabolize PAH (37). Our findings would indicate that the BSMI polymorphism is either acting independent of a lead pathway on adduct formation or that BSMI might be important to adduct formation when body lead stores are low.

Overall our findings suggest that housing status, including census tract home ownership and age of housing, should be further studied in regard to PAH adduct levels and general DNA damage in prostate cancer. In addition zinc intake, lead exposure and the BSM1 polymorphism of the vitamin D receptor may also be important in racial differences in DNA damage pathways.

III. Key Research Accomplishments

Task 1. to determine whether selected *area housing and individual housing status (homeownership, housing density, and other housing factors such as age of structure and heating sources)* are associated with prostate cancer risk, age at diagnosis, and tumor aggressiveness and whether housing status is associated with observed racial differences in these prostate cancer outcomes.

a. Geocoding and retrieval of census housing data was completed (Yr 1).
b. Completed capture of individual level housing variables (Yr 1 and 2).
c. We did not conduct survival analysis. In Year 1 it was determined that a cohort would need to be established. Instead we assessed PSA level at diagnosis as a fourth outcome.
d. Race stratified analyses were conducted.

Task 2. To determine, through the use of factor analysis, whether *area housing and individual housing status*, is associated with prostate cancer risk, age at diagnosis, and tumor aggressiveness, through "latent factors" that include diet, physical activity, and genetic polymorphisms and whether those "latent factors" differ by race.

a. Instead of conducting factor analysis, a two step logistic regression process was used to incorporate a comprehensive set of intermediate and proximal covariates.
b. Race stratified analyses were conducted. In addition, results were stratified by common comorbid conditions.

Task 3. To <u>begin</u> to test biological pathways through which *housing status* may impact prostate health outcomes; specifically, whether *housing status* is associated with markers of DNA damage (polycyclic aromatic hydrocarbons DNA-adducts (PAH)) and DNA stability (telomere content) in prostate tumor tissue and tumor-adjacent normal tissue of African-American and white cases.

a. Housing and PAH- adduct associations were assessed. The sample size for telomeres was too small to assess any significant difference by housing status.

b. Race and comorbidity stratified analyses were conducted.

Task 4. Reporting of results

a. An abstract was presented in poster format at the AACR Science of Cancer Health Disparities meeting in Carefree, Arizona in February 2009. (Appendix 1)

b. Manuscripts are not complete at this time but are in preparation. Manuscripts will be completed as soon as the dissertation is successfully defended.

c. Dissertation defense is anticipated in May 2009. Drafts of the document have been submitted to committee members for review.

IV. Reportable Outcomes

Abstract

Connecting Sociology to Biology: Applying Fundamental Social Cause Theory
To Address Race Disparities in Prostate Cancer. **C. Neslund-Dudas** and B. Rybicki.
AACR Science of Cancer Health Disparities, Carefree Arizona, February 2009.
(see abstract, Appendix 1)

Presentations

The Henry Ford Health System Health Disparities Research Collaborative hosted visits by David Williams, Ph.D. (January x, 2009) and Nancy Krieger, Ph.D. (March 6, 2009), two preeminent health disparities researchers. I was asked to present results from this project during both visits. The presentations were well received and allowed me to thank the two scientists for papers they had written which inspired this project (3;38).

Degrees Obtained

I am in the final phase of dissertation preparation and committee review
and anticipate defending my dissertation in May 2009.

Funding Applied for

A proposal entitled *Residential segregation and lead exposure in prostate cancer race disparities: connecting what we know* was submitted to the Transitioning Investigator disparities announcement of the Department of Defense Prostate Research Program (Summer 2008). The proposal was scored as excellent but not funded.

Employment and Research Opportunities

- In May after defending my dissertation, I will be taking a position as Assistant Research Scientist in the Department of Biostatistics and Research Epidemiology at Henry Ford Health System. As a direct result of this project, a portion of my salary will be covered by the HFHS Health Disparities Research Collaborative headed by disparities researcher, Christine Joseph, PhD.

- I applied for and was accepted to the Junior Scholars Program of the HMO Cancer Research Network (NCI, PI: Edward Wagner, MD). The program is an 18 month intensive mentorship program for new faculty of CRN member organizations. The goal of the program is to develop cancer researchers and is directed by Suzanne Fletcher, M.D. and Robert Fletcher, M.D. Dr. Robert Fletcher will be my mentor through the duration of the program.

- I also recently applied for associate level membership to the American Association for Cancer Research and was accepted.

V. Conclusion

This study which assessed housing status in relation to prostate cancer risk and aggressiveness and DNA damage has provided initial evidence that residential segregation may indeed be a fundamental social cause of race disparities in prostate cancer outcomes, in particular disease aggressiveness. The study also identified lead and PAH adducts as two potential pathways for future studies of housing status and prostate cancer etiology and outcome. The study also highlights the importance of accounting for other comorbid conditions that are likely linked to racial residential segregation. There are already known technologies and processes for lead abatement in homes and for lead chelating therapy. If future studies confirm our findings, lead exposure may become a new target for efforts to reduce prostate cancer disparities. From our findings on occupational lead exposure and commonly studied genetic polymorphisms, we have also learned that lead may be hindering researches abilities to find other causes of the disease and may explain some of the variations in genetic polymorphism findings across populations.

VI. References

1. American Cancer Society. Cancer Facts & Figures for African Americans 2007-2008. 2007. Atlanta, American Cancer Society.

2. American Cancer Society. Cancer Facts & Figures 2008. 2008. Atlanta, American Cancer Society.

3. Williams DR, Collins C. Racial residential segregation: a fundamental cause of racial disparities in health. *Public Health Rep.* 2001;116:404-16.

4. Link BG, Phelan J. Social conditions as fundamental causes of disease. *J Health Soc.Behav.* 1995;Spec No:80-94.

5. Macintyre S, Ellaway A, Hiscock R, Kearns A, Der G, McKay L. What features of the home and the area might help to explain observed relationships between housing tenure and health? Evidence from the west of Scotland. *Health Place.* 2003;9:207-18.

6. Windle GS, Burholt V, Edwards RT. Housing related difficulties, housing tenure and variations in health status: evidence from older people in Wales. *Health Place.* 2006;12:267-78.

7. Krieger N, Chen JT, Waterman PD, Soobader MJ, Subramanian SV, Carson R. Choosing area based socioeconomic measures to monitor social inequalities in low birth weight and childhood lead poisoning: The Public Health Disparities Geocoding Project (US). *J Epidemiol Community Health* 2003;57:186-99.

8. Sargent JD, Bailey A, Simon P, Blake M, Dalton MA. Census tract analysis of lead exposure in Rhode Island children. *Environ Res* 1997;74:159-68.

9. Kerr LR, Grimm MS, Silva WA, Weinberg J, Emerman JT. Effects of social housing condition on the response of the Shionogi mouse mammary carcinoma (SC115) to chemotherapy. *Cancer Res* 1997;57:1124-8.

10. Kerr LR, Wilkinson DA, Emerman JT, Weinberg J. Interactive effects of psychosocial stressors and gender on mouse mammary tumor growth. *Physiol Behav* 1999;66:277-84.

11. Kerr LR, Hundal R, Silva WA, Emerman JT, Weinberg J. Effects of social housing condition on chemotherapeutic efficacy in a Shionogi carcinoma (SC115) mouse tumor model: influences of temporal factors, tumor size, and tumor growth rate. *Psychosom.Med* 2001;63:973-84.

12. Kerr LR, Andrews HN, Strange KS, Emerman JT, Weinberg J. Temporal factors alter effects of social housing conditions on responses to chemotherapy and hormone levels in a Shionogi mammary tumor model. *Psychosom.Med* 2006;68:966-75.

13. Strange KS, Kerr LR, Andrews HN, Emerman JT, Weinberg J. Psychosocial stressors and mammary tumor growth: an animal model. *Neurotoxicol.Teratol.* 2000;22:89-102.

14. Boyle DJ, Hassett-Walker C. Individual-Level and Socio-Structural Characteristics of Violence: An Emergency Department Study. *J Interpers.Violence* 2008.

15. Sayre JW, Katzel MD. Household surface lead dust: its accumulation in vacant homes. *Environ Health Perspect.* 1979;29:179-82.

16. Umbach DM, Weinberg CR. Designing and analysing case-control studies to exploit independence of genotype and exposure. *Stat Med* 1997;16:1731-43.

17. O'Brien PC. The appropriateness of analysis of variance and multiple-comparison procedures. *Biometrics* 1983;39:787-94.

18. Gsur A, Preyer M, Haidinger G, Zidek T, Madersbacher S, Schatzl G et al. Polymorphic CAG repeats in the androgen receptor gene, prostate-specific antigen polymorphism and prostate cancer risk. *Carcinogenesis* 2002;23:1647-51.

19. Mononen N, Ikonen T, Autio V, Rokman A, Matikainen MP, Tammela TL et al. Androgen receptor CAG polymorphism and prostate cancer risk. *Hum Genet* 2002;111:166-71.

20. Hsing AW, Gao YT, Wu G, Wang X, Deng J, Chen YL et al. Polymorphic CAG and GGN repeat lengths in the androgen receptor gene and prostate cancer risk: a population-based case-control study in China. *Cancer Res* 2000;60:5111-6.

21. Platz EA, Leitzmann MF, Rifai N, Kantoff PW, Chen YC, Stampfer MJ et al. Sex steroid hormones and the androgen receptor gene CAG repeat and subsequent risk of prostate cancer in the prostate-specific antigen era. *Cancer Epidemiol Biomarkers Prev* 2005;14:1262-9.

22. Giovannucci E, Liu Y, Willett WC. Cancer incidence and mortality and vitamin D in black and white male health professionals. *Cancer Epidemiol Biomarkers Prev* 2006;15:2467-72.

23. Kemp FW, Neti PV, Howell RW, Wenger P, Louria DB, Bogden JD. Elevated blood lead concentrations and vitamin D deficiency in winter and summer in young urban children. *Environ Health Perspect.* 2007;115:630-5.

24. Rybicki BA, Neslund-Dudas C, Nock NL, Schultz LR, Eklund L, Rosbolt J et al. Prostate cancer risk from occupational exposure to polycyclic aromatic hydrocarbons interacting with the GSTP1 Ile105Val polymorphism. *Cancer Detect.Prev* 2006;30:412-22.

25. Daggett DA, Oberley TD, Nelson SA, Wright LS, Kornguth SE, Siegel FL. Effects of lead on rat kidney and liver: GST expression and oxidative stress. *Toxicology* 1998;128:191-206.

26. Strange RC, Fryer AA. The glutathione S-transferases: influence of polymorphism on cancer susceptibility. *IARC Sci Publ.* 1999;231-49.

27. Hu H, Aro A, Payton M, Korrick S, Sparrow D, Weiss ST et al. The relationship of bone and blood lead to hypertension. The Normative Aging Study. *JAMA* 1996;275:1171-6.

28. Tsaih SW, Korrick S, Schwartz J, Amarasiriwardena C, Aro A, Sparrow D et al. Lead, diabetes, hypertension, and renal function: the normative aging study. *Environ Health Perspect.* 2004;112:1178-82.

29. Sorel JE, Heiss G, Tyroler HA, Davis WB, Wing SB, Ragland DR. Black-white differences in blood pressure among participants in NHANES II: the contribution of blood lead. *Epidemiology* 1991;2:348-52.

30. Anderson LA, Jr. A review of blood lead results from the Third National Health and Nutrition Examination Survey (NHANES III). *Am Ind.Hyg.Assoc J* 1995;56:7-8.

31. Den HE, Nawrot T, Staessen JA. The relationship between blood pressure and blood lead in NHANES III. National Health and Nutritional Examination Survey. *J Hum Hypertens.* 2002;16:563-8.

32. Rybicki BA, Rundle A, Savera AT, Sankey SS, Tang D. Polycyclic aromatic hydrocarbon-DNA adducts in prostate cancer. *Cancer Res.* 2004;64:8854-9.

33. Bieler CA, Wiessler M, Erdinger L, Suzuki H, Enya T, Schmeiser HH. DNA adduct formation from the mutagenic air pollutant 3-nitrobenzanthrone. *Mutat.Res* 1999;439:307-11.

34. Arlt VM. 3-Nitrobenzanthrone, a potential human cancer hazard in diesel exhaust and urban air pollution: a review of the evidence. *Mutagenesis* 2005;20:399-410.

35. Theppeang K, Schwartz BS, Lee BK, Lustberg ME, Silbergeld EK, Kelsey KT et al. Associations of patella lead with polymorphisms in the vitamin D receptor, delta-aminolevulinic acid dehydratase and endothelial nitric oxide synthase genes. *J Occup Environ Med* 2004;46:528-37.

36. Schwartz BS, Stewart WF, Kelsey KT, Simon D, Park S, Links JM et al. Associations of tibial lead levels with BsmI polymorphisms in the vitamin D receptor in former organolead manufacturing workers. *Environ Health Perspect.* 2000;108:199-203.

37. Vakharia DD, Liu N, Pause R, Fasco M, Bessette E, Zhang QY et al. Effect of metals on polycyclic aromatic hydrocarbon induction of CYP1A1 and CYP1A2 in human hepatocyte cultures. *Toxicol.Appl.Pharmacol.* 2001;170:93-103.

38. Krieger N, Emmons KM, White KB. Cancer disparities: developing a multidisciplinary research agenda - preface. *Cancer Causes Control* 2005;16:1-3.

Appendix 1

Abstract presented at AACR Science of Cancer Health Disparities
Carefree, Arizona
February, 2009

Connecting Sociology to Biology: Applying Fundamental Social Cause Theory to Address Race Disparities in Prostate Cancer

Christine Neslund-Dudas and Benjamin A. Rybicki
Department of Biostatistics and Research Epidemiology, Henry Ford Health System, Detroit, MI

Prostate cancer accounts for 37% of all cancers diagnosed in African American men compared to 25 % of cancers diagnosed among men of all races and African American men are 2.4 times more likely than white men to die of the disease. After much research race, age, family history of prostate cancer and living in a Westernized nation are the only consistently recognized risk factors for the disease. Most race disparities research to date has simply taken genes and/or exposures previously examined in predominantly white populations and re-conducted studies in African-Americans. These studies have not taken into account larger social factors that may explain disparities in prostate cancer. Fundamental Social Cause Theory holds that social factors play a role in an individual's ability to avoid disease or manage a disease once it is present. A fundamental social cause influences multiple resources, multiple risk factors and leads to multiple diseases. Factors such as socioeconomic status and residential segregation have been proposed as potential fundamental social causes of disease disparities. Racial residential segregation, in particular, leads to lower quality housing, neighborhoods, education, employment and health care for African-Americans. Prostate cancer is a complex disease that is often described as a "multi-hit" process and therefore, research on prostate cancer disparities may benefit from the application of Fundamental Social Cause Theory. We present an application of the theory using residential segregation as a potential fundamental social cause of prostate cancer disparities. We report associations for African American and white prostate cancer cases and controls that were enrolled in the *Gene-Environment Interaction in Prostate Cancer Study* (GECAP). We report associations for area and individual level factors and disease risk and aggressiveness.

Appendix 2

Current Curriculum Vitae

CURRICULUM VITAE
Christine M. Neslund-Dudas

PERSONAL INFORMATION

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RESEARCH INTERESTS

Exploring the social and biological factors that work in concert to produce race disparities in health. Areas of interest include: African-American disparities in health, neighborhoods and health, prostate cancer, lung cancer, and end-of-life care and the influence of comorbidity on cancer etiology, diagnosis and progression.

EDUCATION

Wayne State University	BS	1988	Biology
Wayne State University	MAT	1994	Secondary Science Education
Wayne State University	Non-degree coursework	1996-1999	Community Medicine (Biostat/Epidemiology)
Wayne State University	PhD	Anticipated Summer 2009	Medical Sociology

PROFESSIONAL EXPERIENCE

1988-1994: Infection Control Technician, Hospital Epidemiology, Henry Ford Health System, Detroit

1994-1997: Project Coordinator, Cntr for Health System Studies, Henry Ford Health System, Detroit

1997-1999: Sr. Project Coordinator, Cntr for Health System Studies, Henry Ford Health System, Detroit

1999-2001: Epidemiologist I, Josephine Ford Cancer Center, Henry Ford Health System, Detroit

PROFESSIONAL EXPERIENCE (CONTINUED)

2001-2006: Epidemiologist II, Biostatistics Research Epidemiology/ Cancer Epidemiology Prevention and Control, Henry Ford Health System, Detroit

2007-present: Epidemiologist III, Biostatistics Research Epidemiology/ Cancer Epidemiology Prevention and Control, Henry Ford Health System, Detroit

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Henry Ford Health System Research Symposium, Abstract Selected for Presentation (2005)

PUBLISHED MANUSCRIPTS

Tammemagi CM, **Neslund-Dudas C**, Simoff M, Kvale P. Impact of comorbidity on lung cancer survival. *International Journal of Cancer,* 2003; 103(6): 792-802.

Tammemagi CM, **Neslund-Dudas C**, Simoff M, Kvale P. Smoking and lung cancer survival - the role of comorbidity and treatment. *Chest,* 2004; 125(1): 27-37.

Tammemagi CM, **Neslund-Dudas C**, Simoff M, Kvale P. In lung cancer patients, age, race-ethnicity, gender and smoking predict adverse comorbidity, which in turn predicts lung cancer treatment and survival. *Journal of Clinical Epidemiology,* 2004; 57: 597-609.

Tammemagi CM, **Neslund-Dudas C**, Simoff M, Kvale P. Lung cancer symptoms - an independent predictor of survival and important mediator of African American disparity in survival. *Cancer*, 2004;101(7):1655-63.

Tammemagi CM, Nerenz D, **Neslund-Dudas C**, Feldkamp C, Nathanson D. Comorbidity & Reduced Survival in African American Breast Cancer Patients, *JAMA,* 2005; 294(14):1765-72.

Hornbrook MC, Hart G, Ellis JL, Bachman DJ, Ansell G, Greene SM, Wagner EH, Pardee R, Schmidt MM, Geiger A, Butani AL, Field T, Fouayzi H, Miroshnik I, Liu L, Diseker R, Wells K, Krajenta R, Lamerato L, **Neslund-Dudas C.** Building a virtual cancer research organization. *J Natl Cancer Inst Monog,* 2005; 35:12-25.

Lambing A, Markey C, **Neslund-Dudas C**, Bricker, L. CD-ROM *Completing A Life*: Comfort Level & Ease Of Use Among Seriously Ill Patients. *Oncology Nursing Forum,* 2006; 33(5):999-1006

Rybicki BA, **Neslund-Dudas C**, Nock NL, Schultz LR, Eklund L, Rosbolt J, Bock CH, Monaghan KG. Prostate Cancer Risk from Occupational Exposure to Polycyclic Aromatic Hydrocarbons is Mediated by the GSTP1 Ile105Val Polymorphism. *Cancer Detect Prev, 2006;* 30(5):412-22.

PUBLISHED MANUSCRIPTS (CONTINUED)

Rolnick SJ, Jackson J, Nelson W, Butani A, Herrinton LJ, Hornbrook M, Bachman D, **Neslund-Dudas C**, Coughlin SS. Pain Management in the Last Six Months of Life Among Women Who Died of Ovarian Cancer. *J Pain Symptom Management, 2007; 33(1):24-31*.

Herrinton LJ, Hornbrook M, Rolnick SJ, **Neslund-Dudas C**, Bachman D, Jackson J, Coughlin SS. Complications at the End of Life in Ovarian Cancer. *J Pain Symptom Management, 2007; 34(3):237-43.*

Jackson J ,Rolnick SJ, Coughlin SS, **Neslund-Dudas C**, Hornbrook M, Darbinian J, Bachman D, Herrinton L. Social Support Among Women Who Died of Ovarian Cancer. *Supportive Care in Cancer,2007;33(1):24-31.*

Tang D, Lui JJ, Rundle A, **Neslund-Dudas C**, Bock CH, Nock NL, Yang JJ, Rybicki BA. Grilled Meat Consumption and PhIP-DNA Adducts in Prostate Carcinogenesis. *Cancer Epidemiol Biomarkers Prev*, 2007; 16(4):803-8.

Nock NL, Tang D, Rundle A, **Neslund-Dudas C**, Savera AT, Bock CH, Monaghan KG, Koprowski A, Mitrache N, Yang JJ, Rybicki BA. Associations Between Smoking, Polymorphisms in Polycyclic Aromatic Hydrocarbon (PAH) Metabolism and Conjugation Genes and PAH-DNA Adducts in Prostate Tumors Differ by Race. *Cancer Epidemiol Biomarkers Prev*, 2007; 16(6):1236-45.

Neslund-Dudas C, Bock CH , Monaghan K, Nora L. Nock, Yang JJ, Rundle A, Tang D, Rybicki BA. SRD5a2 and HSD3B2 Polymorphisms are Associated with Prostate Cancer Risk and Aggressiveness. *Prostate*, 2007; 67(15):1654-63.

Tang D, Lui JJ, , Bock CH, **Neslund-Dudas C**, Rundle A, Savera AT, Yang JJ, Nock NL, Rybicki BA. Racial Differences in Clinical and Pathological Associations with PhIP-DNA Adducts in Prostate. *Int J Cancer*, 2007; 121(6):1319-24.

Rybicki BA, **Neslund-Dudas C**, Bock CH, Rundle A, Savera AT, Yang JJ, Nock NL, Tang D. Polycyclic Aromatic Hydrocarbon—DNA Adducts in Prostate and Biochemical Recurrence After Prostatectomy. *Clin Cancer Res*, 2008;14(3):750-7.

Aiello Bowles EJ, Tuzzio L, Ritzwoller DP, Williams A, Ross T, Wagner EH, **Neslund-Dudas C**, Altschuler A, Quinn V, Hornbrook M, Nekhlyudov L. Accuracy and complexities of using automated clinical data for capturing chemotherapy administrations: implications for future research. (*In press Medical Care*)

Beebe-Dimmer JL, Nock NL, **Neslund-Dudas C**, Rundle A, Bock CH, Tang D, Jankowski M, Rybicki BA. Racial Differences in Risk of Prostate Cancer Associated with Metabolic Syndrome. *(In press Urology)*

SUBMITTED AND IN PREPARATION MANUSCRIPTS

Bock CH, Schwartz AG, Ruterbusch JJ, Levin AM, **Neslund-Dudas C**, Land SJ, Wenzlaff AS, Reich D, McKeigue P, Chen W, Heath EI, Powell IJ, Kittles RA, Rybicki BA. Results from a Prostate Cancer Admixture Mapping Study in African American Men. (*submitted to Urology*)

Nerenz DR, Bennett J, Liang J, Lafata JE, Johnson CC, **Neslund-Dudas C**, Yood MU, Tammemagi CM. Path Analysis as an Approach to Understanding Racial/Ethnic Disparities in Health Care. (In preparation)

ABSTRACTS AND PRESENTATIONS

Rolnick S, Herrinton L, **Neslund-Dudas C,** Bohlke K, Hornbrook M, Coughlin SS. Data Collection For A Pilot Study Of End Of Life Care In Managed Care Systems For Women Who Die Of Ovarian Cancer. *American Society of Preventive Oncology Annual Meeting*. Bethesda, Maryland. March 15th, 2004

Rybicki B, **Neslund-Dudas C**, Sankey S, Thomas D, Monaghan K, Amend K. Interaction between Dietary Fat Intake and the Androgen Receptor CAG Repeat Polymorphism in Prostate Cancer. *Society for Epidemiological Research***.** Salt Lake City, Utah. June 2004.

Neslund-Dudas C, Schultz L, Monaghan K, Bock C, Rybicki B. 3 Beta-Hydroxysteroid Dehydrogenase Type II Polymorphism, Age And Race In Prostate Cancer. *Gerontology Society of America*. Orlando, FL. Nov 18-21, 2005

Herrinton LJ, Hornbrook M, Rolnick SJ, **Neslund-Dudas C**, Bachman D, Jackson J, Coughlin SS. Ovarian Cancer Palliative Care Study: Preliminary Findings. *CDC.* Atlanta, GA. June 2005

Rolnick S, Jackson J, Nelson W, Butani A, Herrinton LJ, Hornbrook M, Bachman D, **Neslund-Dudas C**, Coughlin S. Pain Management in the Last Six Months of Life for Women Who Died of Ovarian Cancer. *American Society of Preventive Oncology (30th Annual Meeting).* Bethesda, Maryland. February 26-28, 2006

Rybicki B**, Neslund-Dudas C,** Savera A, Rundle A, Nock N, Bock C, Yang JJ, Tang D. Polycylic Aromatic Hydrocarbon-DNA adduct Levels are e Predictor of Biochemical Recurrence in Prostate Cancer Patients undergoing prostatectomy. *American Assoc. for Cancer Research*. Charleston, South Carolina. January 11-15, 2006.

Neslund-Dudas C, Krajenta R, Jacobsen G, Hornbrook MC, Bachman DJ, Rolnick SJ, Jackson J, Coughlin SS, Herrinton LJ. Comorbidity and Symptoms in Women Dying of Ovarian Cancer. *HMO Research Network Conference (12th Annual).* Boston, MA. May 1-3, 2006.

Neslund-Dudas C, Tang D, Savera A, Rundle A, Bock CH, Rybicki BA. Race-Specific Determinants of PhIP-DNA Adducts in Prostate Cancer. *HFHS Research Symposium (3rd Annual).* Detroit, MI. April 21, 2006.

Krajenta R, Jacobsen G, Hornbrook MC, Bachman DJ, Rolnick SJ, Coughlin SS, Herrinton LJ, **Neslund-Dudas C.** Comorbidity and Symptoms in Women Dying of Ovarian Cancer. *HFHS Research Symposium (3rd Annual)*. Detroit, MI. April 21, 2006.

ABSTRACTS AND PRESENTATIONS (CONTINUED)

Hornbrook MC, Bachman DJ, Herrinton LJ, **Neslund-Dudas C**, Rolnick SJ. Concentration of Medical Care Utilization at End-of-Life for Ovarian Cancer Patients. *HMO Research Network Conference (12th Annual).* Boston, MA. May 1-3, 2006.

Jackson JM, Rolnick SJ, Coughlin SS, **Neslund-Dudas C**, Hornbrook MC, Darbinian J, Bachman DJ, Herrinton LJ. Social Support Among Women Who Died of Ovarian Cancer. *HMO Research Network Conference (12th Annual).* Boston, MA. May 1-3, 2006.

Neslund-Dudas C, Dudas SP, Meeker AK, Zhang X, Savera AT, Rybicki BA.
A Pilot Study of Telomere Repeat Binding Factor 1 (TRF1) Protein Expression in Prostate Tumor and Adjacent Non-tumor Cells of African-Americans and Caucasians. *AACR Translational Research at the Aging and Cancer Interface*. San Diego, CA. Feb 20-23, 2007.

Neslund-Dudas C, Dudas SP, Meeker AK, Zhang X., Savera AT, Rybicki BA.
A pilot study of telomere repeat binding factor 1 (TRF1) protein expression
in prostate tumor and adjacent non-tumor cells of African-Americans and Caucasians.
Henry Ford Health System Research Symposium, Detroit, MI, Apr 13, 2007

Neslund-Dudas C, Tang D, Bock CH, Rundle A, Nock N, Beebe-Dimmer J, Rybicki BA.
Coffee, beer, and wine consumption and PhIP-DNA adducts in black and white men with prostate cancer. *AACR - The Science of Cancer Health Disparities, Atlanta, GA, Nov 27-30, 2007*

Neslund-Dudas C, Dudas SP, Meeker AK, Zhang X, Savera AT, Mikita R, Rybicki BA.
A pilot study of telomere repeat binding factor 1 (TRF1) and telomere content in prostatectomy specimens of black and white men with prostate cancer. *AACR – Telomeres and Telomerase in Cancer, San Francisco, CA, Dec 6-9, 2007*

Neslund-Dudas C, Jankowski M, Levin A, Datta I, Rybicki BA. htSNP in the endothelin axis and prostate cancer risk and aggressivness in African-American and white men . *AACR –Advances in Prostate Cancer Research, San Diego, CA, Jan 21-24, 2009.*

Neslund-Dudas C, Rybicki BA. Connecting Sociology to Biology: Apply Fundamental Social Cause Theory to prostate cancer race disparities. *AACR-The Science of Cancer Health Disparities, Carefree, AZ, Feb 3-6, 2009.*

Bock CH, Schwartz AG, Ruterbusch J, **Neslund-Dudas C**, Land S, Reich D, McKeigue P, Chen W, Heath EI, Kittles RA, Rybicki BA. Prostate cancer susceptibility loci: results from admixture mapping study in African American men. *AACR-The Science of Cancer Health Disparities, Carefree, AZ, Feb 3-6, 2009.*

CURRENT FUNDING

Department of Defense –Pre-Doctoral Training Grant Neslund-Dudas(PI) 3/15/ 2007-3/14/2009
W81XWH-07-1-0252
Role: PI
Residential Segregation, Housing Status, and Prostate Cancer in African-American and White Men
This training grant is assessing the relationship between individual and area measures of housing and prostate cancer outcomes (age at diagnosis, aggressiveness, recurrence) in African-American and White Men. The study is using previously enrolled and well defined prostate cancer cases, diagnosed at a large health system serving the Metropolitan Detroit Area.

NIH/NIEHS Rybicki (PI) 6/01/07-2/28/12
R01 ES011126-06 A2
Role: Project Manager
Nested Case Control Study of Prostate Carcinogenesis
The primary aims of this study are 1) to determine whether biomarkers of DNA damage (PAH-andPhIP-DNA adducts) are predictive of prostate cancer (CaP) development, 2) to determine in a multivariable model how known markers of progression to CaP (i.e., DNA methylation affect the association between PAH-and PhIP-DNA adducts and prostate cancer and 3) to determine whether DNA adducts in the benign prostate are associated with the level of expression of p53 and p21waf/cip1 tumor suppressor genes in subsequent prostate tumors.

R01 CA088164-07A2 Witte (PI) 12/01/06-11/30/11
Role: HFHS Project Manager
Genetic Epidemiology of Prostate Cancer Aggressiveness
The purpose of this application is to evaluate the impact of candidate genes involved with the innate immunity and inflammation pathway and nonsteroidal anti-inflammatory drugs (NSAIDs) on prostate cancer development and progression.

OTHER RECENT SUPPORT

NIH/NIEHS 5 R01 ES11126-03 Rybicki (PI) 9/30/00 – 7/31/05
Role: Project Manager
Gene-Environment Interaction in Prostate Cancer
The objective of this project is to identify combinations of genetic and environmental risk factors that increase a man's risk for prostate cancer above what would be expected if the risk factors acted independent of each other. Hypotheses are focused on occupational and dietary risk factors and the genes that may modify them based on our current understanding of prostate carcinogenesis.

CDC Task Order 200-95-0953-953-047 10/1/2000-9/30/2002
Role: HFHS Site PI
Evaluation of End-of-Life Care for Prostate Cancer in the Managed Care Environment
This retrospective study enrolled nearly 500 subjects who had died of prostate cancer between 1993 and 2000. Medical records including inpatient, outpatient and hospice data were abstracted. Participating sites included Group Health Cooperative (Seattle) and Henry Ford Health System (Detroit).

OTHER RECENT SUPPORT (CONTINUED)

NCI 5U01CA093332-04 Weeks (PI) 9/18/01-8/31/06
Role: HFHS Project Manager (2001-2004)
Lung/Colon Cancer Outcomes--Cancer Research Network
This RFA cooperative agreement (RFA-CA-01-013) supports a new collaborative research consortium to conduct Cancer Care Outcomes Research and Surveillance (CanCORS), NCI's first major step to support the development of a system for obtaining details about cancer care beyond the initial diagnosis and limited treatment data that are now routinely collected in high quality population-based cancer registries. This research will help build the information base needed for measuring and improving the quality of cancer care in the US. CanCORS purpose will be to collaboratively collect and analyze process-outcome relationships in patients newly diagnosed with lung or colorectal cancer.

CDC Task Order 2002-Q-00654 10/1/2002-1/31/2006
Role: HFHS Site PI
Evaluation of Hospice Referral and Palliative Care for Ovarian Cancer in the Managed Care Environment
This retrospective study is evaluating end-of-life care for women who died of ovarian cancer. Participating sites include Kaiser Permanente Northern California, Kaiser Permanente Northwest, and Henry Ford Health System. Data has been collected for more than 400 women and is now being analyzed

NIH/NIEHS 3 R01 ES011126-02S1 Rybicki (PI) 8/1/02 – 7/31/05
Role: Project Manager
Determinants of PAH-DNA Adducts in Prostate Cancer
The main objective of this project is to identify combinations of genetic and environmental risk factors that determine levels of polycyclic aromatic hydrocarbon (PAH) DNA adducts in prostate cancer tissue.

NCI U19 CA 79689 Wagner (PI), CC Johnson (HFHS Site-PI) 3/1/03 – 2/28/07
Role: HFHS Project Manager Infrastructure
Increasing Effectiveness of Cancer Control Interventions: HMO Cancer Research Network:
The goal of this program is to determine and improve the effectiveness of cancer control interventions that span the natural history of major cancers among diverse populations and health systems.

Karmanos Cancer Institute –Strategic Research Initiative Rybicki (Acting PI) 1/1/2006-12/31/2006
Role: Grant Author/ PI
Race Disparities In Prostate Cancer: Do Telomeres Play A Role?
Research on telomeres as biomarkers of prostate cancer and as biomarkers of socioeconomic impact on health are converging to highlight the potential importance of telomere assessment in health disparities research in PCa. The objectives of this pilot study are to demonstrate our ability to quantify and assess telomere content using paraffin embedded tumor and tumor-adjacent normal tissue of prostate cancer cases and begin to determine if there are associations between race and telomere content in prostate tissue. Also, we will demonstrate our ability to assess telomere repeat binding factor-one (TRF1) levels in tumor and tumor adjacent-normal prostate tissue and begin to determine if there is an association between TRF1, race and telomere length. (TRF1 is a negative regulator of telomere length.)

Robert Wood Johnson Foundation Nerenz (PI) 4/1/2007- 3/31/2008
Role: Archived Data Support
Reanalyzing data sets using path analysis and structured equation modeling to reduce racial and ethnic health care disparity